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MORGAN, LEWIS & BOCKIUS LLP (SF)
2 PALO ALTO SQUARE
3000 El Camino Real, Suite 700
PALO ALTO, CA 94306

EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/760,003	SOLOW-CORDERO ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *3,19,24 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-18, 20-23, 25-26 and 28-42* is/are rejected.

7)☒ Claim(s) *1-2, 29-33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants Response to Restriction Requirement Acknowledged

1. Applicant's election, with traverse, with the Group I, drawn to a method of modulating an Edg-3 receptor mediated biological activity with carboxamide compounds when X is O , classified in class 514, subclass 613), claims 1-32, along with compound 101 and cardiovascular as the elected species is acknowledged.

Applicants traverse the restriction requirement on the grounds that there would be no burden in searching the entire groups. This argument is not persuasive, as claimed invention would be distinctive, each from the other for the reason of the record. Furthermore, the search of the entire groups in the non-patent literature (a significant part of a thorough examination) would be burdensome. Therefore, the requirement is still deemed proper, and made Final.

The elected species compound 101 is free from prior art, search has been extended to compound read on elected invention (having Edg3 receptor inhibitory activity). The claims have been examined insofar as they readable to the searched compound.

Claims 1-2, 4-18, 20-23, 25-26 and 28-42 read on the elected invention. Claims 3, 19, 24 and 27 are withdrawn from further consideration by the examiner as being drawn to non-elected invention.

Priority

2. It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/440,322 filed January 16, 2003 and 60/454,880 filed March 13, 2003. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the

filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was

unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Claim Objections

3. Claims 1-2 and 33 are objected to because of the following informalities: "selected from" is improper Markush-type language. "selected from" should be corrected as "selected from the group consisting of". Appropriate correction is required.

4. Claims 29-32 are objected to as being incomplete. No structure and definition of compound of formula I or II are depicted in claims 29-32. For the examination purpose, "the formula (I) or (II)" is interpreted as the compound of the formula (I) or (II) in claim 1 or 2.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2, 4-18, 20-23, 26 and 28-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing or activating the specific biological activity (e.g., VEGF synthesis or IL-8 synthesis) or treating the specific cardiovascular disease or cancer, does not reasonably provide enablement for "modulating an Edg-3 receptor medicated biological activity...", "treating or preventing cancers..." or "treating cancers...". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a method for modulating an Edg-3 receptor mediated biological activity or treating or preventing "cancers..." comprising administering a compound of formula (I), (II), (III) or (IV).

Websters II Dictionary defines the term "modulate" as "to adjust or adapt to a certain proporition; to pass gradually from one state to another", "prevent" as "anticipate or counter in advance, to keep from happening" and "inhibit" as "to prevent; to prohibit".

The interpretation of the instant claims, drawn to "a method of modulating an Edg-3 receptor mediated biological activity..." allows for the inhibition (down-regulation), stimulation or enhancement (up-regulation) and/or mixed up and down regulation of an Edg-3 receptor mediated biological activity, whereas the interpretation of the instant claims, drawn to "a method of treating or preventing "cancers..." allows for the complete cure and eradication or total elimination of "cancers..." by the administration of said compounds,

With respect to the scope of enablement for "modulation" (inhibition or prevention) of Edg-3 receptor mediated biological activity or "prevention" of "cancers, acute lung disease... cardiovascular disease...",

Similarly as discussed above, the interpretation of instant claims includes not only the modulation (e.g., inhibition and/or activation) of Edg-3 receptor mechanism, but also the treatment or prevention of any diseases or conditions associated or involved with Edg-3 receptor mechanism by administering the compounds represented by the formula (I) or (II).

There are no known compounds of similar structure which have been demonstrated to prevent or cure any diseases or biological activities by Edg-3 receptor mechanism. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merit. For example, there is no known cure for cancers or cardiovascular diseases. The true fact of the state of the art is illustrated succinctly in the ("NIH

Heart Disease & Stroke Research: Fact Sheet", American Heart Association, 2004; "Cardiovascular Disease: Treatment for Stroke", Stanford Hospital & Clinics, 2003; "Heart Disease", Charlotte E. Grayson, WebMD, 2004; "Acute Congestive Heart Failure", Thomas N. Levin, Postgraduate Medicine, Vol. 101, No. 1, 1997; "Baylor, St. Luke's study uses gene therapy as pancreatic cancer", April Sutton, www.bcm.edu, 2006; "Drugs hold promise in kidney cancer fight", Marchione et al., www.ledger-enquireer.com, 2006). Thus, it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" or completely cure or eradication effect.

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmacy art is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the preventive utility of the instant compounds.

The specification provides assays to test compounds of the Formula I or II, particularly compound 101in vitro and discloses that compound 101 exhibits Edg-3 receptor inhibitory properties (Example 2). However, there is no demonstrated correlation that the tests and results apply to the claimed preventive utility embraced by the instant claims.

Since the efficacy of the claimed compound(s) in preventing the claimed conditions (for example cancers or cardiovascular diseases) mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

With respect to the scope of enablement for the treatment (or prevention) "Edg-3 receptor mediated biological activity", "cancers...cardiovascular diseases" or "cancers",

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5(BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art; In re Wright, 9999 F.2d 1577, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of treating or preventing "Edg-3 receptor mediated biological activity", "cancers, acute lung diseases, acute inflammatory exacerbation..." or "cancer" prior to filling of the instant invention was an unpredictable art.

The scope of the instant invention is extremely broad. The scope of the instant claims encompasses prevention (complete thwarting or warding off illness or total elimination or eradication of disease) or treatment of multiple complex disorders that may have unrelated manifestations including cancers (e.g., ovarian, periotoneal, endometrial, cervical, breast, colorectal, uterine, stomach, small intestine, thyroid, lung, kidney, pancreas and prostate cancer), acute lung diseases, adult respiratory distress syndrome, asthma, cutaneous burns, transcorneal freezing, cardiovascular diseases (e.g., coronary artery disease, heart valve disease, arrhythmia, heart failure, stroke, shock, endocarditis, diseases of the aorta and its braches, disorders of the peripheral vascular systems, congenital heart diseases, angina (particularly chronic, stable angina pectoris), cardiomyopathy, restenosis, ischemic disease, pulmonary edema associated with acute myocardial infarction, thrombosis, platelet aggregation, platelet adhesion, pulmonary thromboembolism, cerebral thromboembolism, arteriovenous fistula, atheroembolism, etc...).

Although the instant invention links Edg-3 mechanism to the pathophysiology of multitude of disease as discussed above, it is not known yet that a single underlying mechanism ties together all of the seemingly unrelated manifestations. Therefore, the skilled artisan would turn to undue amount of trial and error to find out which disease or condition would be response to the administration of said compounds having Edg-3 receptor modulating activity.

The specification provides assays to test compounds of the Formula I or II, particularly compounds 101, in vitro and discloses that compound 101 exhibits Edg-3 receptor inhibitory properties (Example 2). However, there is no demonstrated correlation that the tests and results apply to the treatment of disease conditions embraced by the instant claims. Ex parte Maas, 9

USPQ2d 1746, makes clear "First, although appellants' specification describes certain in vitro experiments, there is no correlation on this record between in vitro experiments and a practical utility in currently available form for humans or animals. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to utility in humans or animals".

As discussed above, no examples exist for efficacy of a single product against all types of diseases or conditions or cancers. For example, Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different method of growth and harm the body. Also see In re Buting, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists or pharamcologists today to get an agent to be effective against "biological activity" or "cancers..." mediated by Edg-7 receptor mechanism. As discussed in preceding comments, the existence of such a "silver bullet" is contrary to our present understanding of oncology or pharmacology.

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re

Fishcher, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575.

As discussed above, considering above factors, especially the "sufficient working examples", "the level of skill in the art", "the relative skill and the unpredictability in the pharmaceutical art", "breadth of the claims" and "the chemical nature of the invention", one having ordinary skill in the art would have to undergo an undue amount of experimentation to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-2, 4-13, 15-16, 22-23, 26, 28-34 and 39, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and unclear of the term "Edg-3 receptor mediated biological activity" and leave the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear. In this regard, although the specific examples (calcium mobilization, VEGF synthesis, etc...) are shown in the specification, it is considered that the meaning of the claims should be clear from the wording of the claim alone.

Regarding claim4, claim 4 recites "an antagonist". The claim is vague and unclear and leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear. What types of antagonist activity does it refer to?

Claims 5-9 and 15-16 recite "other Edg receptors". The claims are vague and unclear and leave the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear. What types of Edg receptors do they refer to as comparing with the compounds of the formula having Edg-3 inhibitory activity? In this regard, although the specific examples (i.e., selectivity for Edg-3 relative to Edg-4 and Edg-7 receptors) are shown in the specification, it is considered that the meaning of the claims should be clear from the wording of the claim alone.

Claims 1 and 33 recite "substituted". The claims are vague and unclear and leave the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear. One of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patient protection desired as to "substituents" encompassed thereby. Given the fact that any significant str uctural variation to a compound would be reasonably expected to alter its properties, e.g., physiological effects and functions, the scope of claim is indefinite as to the compound encompassed thereby. In this regard, although the specific embodiments (i.e., substituted alkyl, susbstitued alkylthio, substituted heteroalkyl, etc...) are shown in the specification, it is considered that the meaning of the claims should be clear from the wording of the claim alone.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

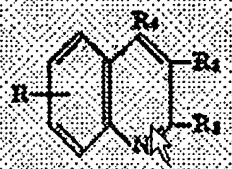
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 4-18, 20-23, 25-26 and 29-42 rejected under 35 U.S.C. 103(a) as being unpatentable over Bickerton (US 3178348) in view of Cecil, Textbook of Medicine, ("Cecil").

Bickerton teaches a method for the treatment of hypertension which comprises the administration of an effective amount to animals of a compound of the formula:



wherein

R is selected from the group consisting of hydrogen and from one to three substituents at positions 5, 6, 7 and 8 of the quinoline nucleus chosen from the group consisting of methoxy, ethoxy and methylmercapto;

R_2 and R_4 are each selected from the group consisting of hydrogen, hydroxy and methyl; and

R_3 is selected from the group consisting of hydrogen and hydroxy and pharmaceutically acceptable salts thereof; as the active ingredient in association with a suitable pharmaceutical carrier.

This compound corresponds to the compound of present claim 28 where the reference teaches R may be at positions 5, 6, 7 and 8 and may be a group selected from the group consisting of methoxy, ethoxy and methylmercapto, (Applicants' $(R_5)_o$ is alkoxy and $_o$ is 1, 2 or 3), R_2 and R_4 are each selected from hydrogen, hydroxy and methyl, (Applicants' R_1 may either be absent or hydrogen, R_2 may be absent, hydrogen, alkyl, and R_4 may be carboxy) and the reference's R_3 may be hydrogen (Applicants' Y may simply be C).

The differences between the above and the claimed subject matter lies in that the patentees fail to

(i) report the compound's effect on Edg-3 receptors as in present claims 1, 2, 4-12, 14-17 and 21-23;

(ii) teach the molecular weight of the compound(s) to be less than 750 daltons, (see present claim 25);

(iii) the cell type which is affected (see present claim 26); and

(iv) the effect of the compound against atherosclerosis, vasoconstriction, vascular occlusive disorders, vasoconstriction in cerebral arteries, stroke or ischemia (present claims 40-45).

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) the compound of Bickerton meets the definition of the compounds of the present claims and the host of the patent is indistinguishable from the present claims, the Examiner has reason to believe that the claimed Edg-3 activities of the present claims were inherent in the prior art compounds, whether expressly disclosed or not, (see MPEP § 2112).

(ii) Because the same compounds of the present claims are those of the prior art, it must logically follow that the molecular weights of the prior art compounds are within the presently claimed requirements,

(iii) the references teaches the administration of the compound and the cell types of the present claims would be present in the host of both the claims and the reference and thus, in the absence of evidence to the contrary, the requirement of present claim 26 would inherently be met by the prior art process; and

(iv) while Bickerton only expressly discloses the treatment of hypertension, one skilled in the art would have appreciated that the compounds disclosed therein would also be effective against the atherosclerosis, vasoconstriction, vascular occlusive disorders, vasoconstriction in cerebral arteries, stroke or vasospasm (present claims 40-45) because these conditions/effects may be associated with hypertension. In particular, Cecil teaches "Hypertension, in concert with other cardiovascular risk factors, leads to atherosclerosis" (page 259, col. 2, second paragraph under the heading "Etiology and Pathogenesis..Cardiovascular Complications"). Additionally, one skilled in the art would have found it logical that vasoconstriction may be associated with hypertension because with a decrease in the vascular lumen for a given rate of blood flow, pressure must rise. Also, with respect to stroke, Cecil teaches "[o]f even greater concern is that the cardiovascular complications of high BP (blood pressure) are increasing: Since 1993, age-adjusted stroke rates have risen..." thus implying that by effective treatment of hypertension, treatment, i.e., a reduction in the incidence, of stroke may be accomplished as well. Finally, concerning ischemia, Bickerton teaches arterial hypertension in general and thus would have included antihypertensive therapy for high-risk groups or those suffering from hypertensive emergencies which include ischemic stroke (see Table 55-10, third entry from the top).

Accordingly, the claims are deemed to be properly rejected.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-2, 4-18, 20-23 and 26, 28-42 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-2, 4-13, 18-27, 39-45, 47 and 51-56 of Copending Application No. 10/390426 or claims 1-2, 4-27 and 29-32 of Copending Application No. 10/760062. This is a provisional obviousness-type double patenting rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claimed invention overlaps to each other.

All of the instant application and the copending applications are directed to a modulating an Edg-3 receptor mediated biological activity or treatment of cardiovascular diseases with administering a compound of the claimed compounds including compound 101.

9. In looking in continuity data, it is noted that applicant has numerous copending applications encompassing the same or similar subject matter of the instant application. Applicant should review all subject matter considered the same or similar, and submit the appropriate Terminal Disclaimer(s). For example, 10/760064, 10/760061, 10/760063, 10/759992, and 10/390427-29 contain to be same or similar subject matter(s).

Conclusion

10. No Claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

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Brian Kwon
Patent Examiner
AU 1614